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The healthcare costs of heart failure during the last five years of life: A retrospective cohort study

William Hollingworth¹; Mousumi Biswas¹; Rachel L Maishman²; Mark J Dayer³; Theresa McDonagh⁵; Sarah Purdy¹; Barnaby C Reeves²; Chris A Rogers²; Rachael Williams⁴; Maria Pufulete²

Affiliations:

1 School of Social and Community Medicine, University of Bristol, Bristol, UK

2 Clinical Trials and Evaluation Unit, School of Clinical Sciences, University of Bristol, Bristol, UK

3 Department of Cardiology, Taunton and Somerset NHS Foundation Trust, Taunton, UK

4 Clinical Practice Research Datalink, Medicines and Healthcare products Regulatory Agency, London, UK

5 King's College Hospital, London, UK

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

Corresponding author:

Professor William Hollingworth
School of Social and Community Medicine,
University of Bristol, Bristol, UK
Tel: +44 117 9287355
Fax: +44 117 9287325
Email: William.hollingworth@bristol.ac.uk

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Conflicts of interest:

RW is an employee of CPRD, who received funding from the University of Bristol to provide access to the data for this study. CPRD provide research services for, and receive associated funding from, a range of pharmaceutical, academic, governmental, NGO and regulatory organisations. MJD has accepted fees for advisory boards from St Jude who make a range of cardiology devices and also from Bayer for support for attending conferences. All other authors declare no conflicts of interest.

Keywords: Health Care Costs; HF; Terminal Care; Hospital Costs;

Abstract:*Background*

Evidence on the economic impact of heart failure (HF) is vital in order to predict the cost-effectiveness of novel interventions. We estimate the health system costs of HF during the last five years of life.

Methods

We used linked primary care and mortality data accessed through the Clinical Practice Research Datalink (CPRD) to identify 1,555 adults in England who died with HF in 2012/13. We used CPRD and linked Hospital Episode Statistics to estimate the cost of medications, primary and hospital healthcare. Using GLS regression we estimated the relationship between costs, HF diagnosis, proximity to death and patient characteristics.

Results

In the last 3 months of life, healthcare costs were £8,827 (95% CI £8,357 to £9,296) per patient, more than 90% of which were for inpatient or critical care. In the last 3 months, patients spent on average 17.8 (95% CI 16.8 to 18.8) days in hospital and had 8.8 (95% CI 8.4 to 9.1) primary care consultations. Most (931/1555; 59.9%) patients were in hospital on the day of death. Mean quarterly healthcare costs in quarters after HF diagnosis were higher (£1,439; [95% CI £1,260 to £1,619]) than in quarters preceding diagnosis. Older patients and patients with lower comorbidity scores had lower costs.

Conclusions

Healthcare costs increase sharply at the end of life and are dominated by hospital care. There is potential to save money by implementation and evaluation of interventions that are known to reduce hospitalisations for HF, particularly at the end of life.

Introduction:

Global estimates indicate that heart failure (HF) results in \$65 billion direct care costs and \$43 billion in lost productivity annually due to morbidity and premature mortality (1). In the UK approximately 500,000 people live with HF (2); this figure is likely to rise as the population continues to age. Each year HF is the primary diagnosis in over 150,000 hospital episodes in the UK (2); many of these are emergency admissions.

Median survival following the first hospitalisation with HF has consistently improved in recent years (3). However prognosis remains poor; five year mortality was 45.5% among patients with an unscheduled hospital admission for HF in England and Wales in 2009(4). Rapid developments in the monitoring and treatment of HF have provided clinicians with many more options in selecting physical, pharmacological (5) and interventional therapies (6). Evidence-based guidelines (7) aim to help clinicians and patients choose the most effective and cost-effective therapies. The case for many novel interventions is based on the presumption that the upfront costs of more intensive therapy will be justified in the longer term by improved patient outcomes and savings due to reduced hospitalisations. Therefore, detailed information on the long-term economic impact of HF is vital in order to accurately predict the true value of therapy.

As part of a wider review (8) of the cost-effectiveness of serum B-type natriuretic peptide monitoring in patients with HF, we aimed to estimate the cost to the health system of treating patients with HF during the last years of life. Specifically, our objectives were to identify the relative contribution of different types of care (i.e. inpatient, outpatient, primary care, and medications) to the overall cost and to determine how cost differs by age (<75 years versus ≥75), proximity to death and underlying cause of death (circulatory versus other).

Methods:

Cohort identification

We retrospectively identified a cohort of patients who died of or with HF from the Clinical Practice Research Datalink (CPRD) primary care database linked to Hospital Episode Statistics (HES) data, and Office for National Statistics (ONS) mortality data. CPRD is a computerised database of anonymised patient primary care records (9). It includes records from over 11 million patients, including 4.4 million 'active' (i.e. alive and GP registered) patients. This is equivalent to approximately 6.9% of the UK population; active patients are representative of the age and sex distribution of the general population.

CPRD contains demographic information, clinical diagnoses, consultations, investigations and prescription data. HES is a routinely collected dataset that records all episodes of care provided to all patients (NHS funded and privately insured) in English NHS hospitals and NHS funded patients treated in English independent sector hospitals (10). HES has separate datasets for admitted patient care (APC), covering day case or inpatient admissions to hospital; adult critical care (CC); outpatient activity (OP), covering outpatient appointments, radiology and procedures; and accident and emergency (A&E). The A&E dataset was introduced in 2007/8 and considered experimental until 2012/13 and is not included in this analysis.

Eligibility criteria were (see Figure 1): 1) patients eligible for CPRD, HES and ONS mortality data linkage; 2) ONS death date between 01/05/2012 and 30/04/2013; 3) any Read code (Appendix) indicating a diagnosis of HF recorded in the CPRD primary care record between 01/05/2010 and 30/04/2013; 4) CPRD quality assessment flags indicated the patient and practice data were 'acceptable' and 'up to standard' for use in research since at least 01/05/2010 (9). We excluded

patients whose HES patient record was linked to more than one CPRD record. We also excluded patients who: were less than 18 years at the time of death; left the practice before death; were not registered with the practice for at least one year prior to death; or where the practice had not uploaded CPRD data since before their death. We defined the HF index date as the earliest date since 01/01/2004 when a primary care Read code or HES/ONS ICD10 code indicated a diagnosis of HF.

Cost of health care

We excluded care provided more than five years before death and the small proportion of care recorded as occurring after death. The latter probably represents data entry error or planned care (e.g. outpatient appointments) not received. We also excluded a small percentage of duplicate records.

Costs of hospital-based care were estimated from HES data. The HES APC data record inpatient and day case episodes provided by one clinical team. HES APC data can be used to identify hospital spells which may contain more than one episode if care is transferred from one clinical team to another while in the same hospital. Numerous methods have been proposed for costing hospital admissions, but there is no gold standard (11). We costed admissions at the level of hospital spell, distinguishing between the fixed costs (e.g. initial surgery) and the variable costs of care as length of stay increases. Costs were estimated based on whether the admission was elective or non-elective (type); more or less than two days (short stay); length of stay (days); and the healthcare resource group (HRG). HRG codes provide information on the chapter (e.g. cardiac), sub-chapter (e.g. cardiac procedures), root (e.g. coronary artery bypass graft) and split (e.g. coronary artery bypass graft with complications/comorbidity score 12+) in order to group clinically and financially similar admissions.

Different versions of HRG codes were introduced over the study period, and the HRG root was not known for some admissions, particularly in earlier years.

Each year hospitals report reference costs and episode numbers by HRG split (12). We performed ordinary least squares regression, weighted by number of episodes to estimate the relationship between 2013/14 reference costs (refcost) for each HRG-split group (i) and the following covariates:

$$\text{refcost}_i = \beta_1 + \beta_2 \text{type}_i + \beta_3 \text{short stay}_i + \beta_4 \text{HRG root}_i + \beta_5 \text{days}_i + \varepsilon_i$$

This provides an estimate of the fixed (β_1 , β_2 , β_3 , and, when available, β_4) and variable (β_5) costs of each HES admission. NHS reference costs include the cost of devices such as implantable cardioverter-defibrillators and cardiac resynchronisation therapy.

English NHS hospitals also report reference costs (12) per critical care day stratified by the number of organs supported. For patients where the maximum number of organs supported was recorded in the HES dataset we used this to calculate average cost per critical care day. For other patients we used the average cost per critical care day for adult patients.

We excluded outpatient appointments that patients cancelled or did not attend. The costs of outpatient appointments were estimated using national reference costs (12). Completeness of diagnostic coding in OP data is low; therefore, we estimated the OP attendance cost using a frequency weighted average of all outpatient reference costs for the specialty. Outpatient procedures are recorded using OPCS procedure codes (13) which we mapped (14) to four character HRG root codes and national reference costs (12) were applied.

To avoid double costing, we excluded primary care events that did not represent direct patient contact (e.g. administration, which is already incorporated as an overhead in national unit costs) and care provided outside of the primary care setting. The remaining primary care contacts were grouped by mode of contact into practice-based contacts, telephone contacts and home or other

out of practice contacts. National unit costs (15) were used to estimate the cost of each contact based on the mode of contact and the staff member (GPs, allied health professionals or other/unknown). The CPRD records all primary care prescriptions, including medicinal products, dressings and other appliances, provided to patients. There is no automated way to link therapies to costs. For prescriptions, we coded the Chapter, Section and Paragraph of the drug on the British National Formulary (BNF) (16) and used prescription cost analysis (17) data to estimate the average cost of a prescription for all drugs within that paragraph of the BNF. We excluded dressings and other appliances from our cost analysis. We excluded primary care investigations (e.g. physical examination) which are a routine part of a consultation and diagnostic procedures which coincided with an outpatient appointment on the assumption that these test costs were included in the HES outpatient dataset. Laboratory tests (e.g. clinical biochemistry; haematology; microbiology) and other diagnostic services (e.g. ECG, imaging) were categorised and national reference costs were applied (12).

We identified hospital care and primary care medications related to diseases of the circulatory system using the HRG chapter ('E') and BNF Chapter ('2') respectively. We were unable to reliably distinguish primary care contacts and investigations related to the circulatory system from those related to other comorbidities as patients often consult GPs with multiple morbidities.

Data analysis

We calculated total secondary and primary care health system use (i.e. hospital days, outpatient contacts, primary care contacts and medications) and costs for each three-month period (quarter) during the last five years of life (i.e. 20 quarters). We identified patients with left ventricular dysfunction based on Read codes recorded in the CPRD and ICD10 diagnosis codes recorded in HES. Comorbidities and the Charlson comorbidities score were calculated using published algorithms(18). We performed two regression analyses using a GLS random-effects model. First, we regressed health

system costs on HF index date and proximity to death (HF cost model). In the second regression (subgroup cost model), we included additional covariates for patient age (<75, ≥75 years at cohort inception), gender, Charlson score, left ventricular dysfunction and underlying cause of death (circulatory [ICD10 chapter IX] / other) to explore the influence of these characteristics on costs. Results are reported as means and 95% confidence intervals (95% CI) unless otherwise specified. Costs are reported in 2013/14 British pounds (£1 = €1.19 = \$1.58 at 2013/14 exchange rates).

Results:

The cohort included 1555 patients with a mean age at the time of death of 83 (10 SD) years (Table 1). Most (931/1555; 59.9%) patients were in hospital on the day of death. Circulatory disease was the underlying cause of mortality recorded for the majority of patients (895/1555; 57.6%), but respiratory system disease and neoplasms were also common causes of death. A small proportion (235/1555; 15.1%) had a HF diagnosis recorded more than five years before death. A large proportion (936/1555; 60.2%) had a HF diagnosis first recorded within two years of death. Left ventricular dysfunction was recorded in just over half of the patients (882/1555; 56.7%).

All types of health care use increased with proximity to death but the pattern varied by service type (Figure 2). Outpatient appointments and medications increased relatively linearly, approximately doubling over the five-year period before death. Patients had a mean of 0.8 (95% CI 0.7 to 0.9) outpatient appointments and 18.3 (95% CI 17.3 to 19.3) medications in quarter 1 compared to 1.6 (95% CI 1.5 to 1.8) appointments and 34.4 (95% CI 32.8 to 36.0) medications prescribed in quarter 20. In contrast the use of primary care consultations and hospital bed days increased most rapidly in the last 6 months of life. During the last 3 months of life, patients spent on average 17.8 (95% CI 16.8 to 18.8) days in hospital and had 8.8 (95% CI 8.4 to 9.1) primary care consultations.

531 (17%) of the 3200 cardiac hospitalisations were elective admissions. 1141 (73.3%) of 1555 patients had at least one cardiac admission (median 1, range 0 to 57). The majority of cardiac hospitalisations were for heart failure (35.1%) or 'non-interventional acquired cardiac conditions' (13.8%) (Table 2). There were 155 admissions related to implantable devices, including 72 for implantation of pacemaker and 26 for implantation of cardioverter defibrillator. Non-cardiac admissions for urinary, respiratory and digestive system problems were common. Patients received a wide array of cardiovascular system medications (Table 2). Most patients had at least one

prescription from the following BNF sections: diuretics (1249/1555; 80.3%); hypertension or HF drugs (1145/1555; 73.6%); antiplatelet drugs (975/1555; 62.7%); beta blockers (894/1555; 57.5%); nitrites or calcium channel blockers (894/1555; 57.5%); or lipid regulators (881/1555; 56.7%).

Inpatient costs dominate health care costs, comprising 60-91% of cost throughout the last 5 years of life (Figure 3). Over the last year of life mean health care costs were £17,945 (95% CI £17,066 to £18,823). Costs during the last year of life were lower in patients where HF was recorded as the underlying cause of death (£17,041 versus £19,171, mean difference £2,130; 95% CI £335 - £3,906) and in patients aged 75 or older at cohort inception (£16,248 versus £22,219, mean difference £5,971; 95% CI £4,045 to £7,898). In the last 3 months of life, health care costs were £8,827 (95% CI £8,357 to £9,296) per patient, more than 90% of which were for inpatient or critical care.

Regression analyses demonstrate that mean quarterly healthcare costs were higher in quarters after HF diagnosis (£1,439; [95% CI £1,260 to £1,619]) than in quarters preceding diagnosis (Table 3; HF cost model). In the subgroup cost model, adjusting for age group, gender, comorbidities, left ventricular dysfunction and cause of death, costs were £6,782 (95% CI £6,289 to £7,275) higher in the final three months of life than in an equivalent period five years before death. Older patients (≥ 75) had less expensive quarterly health care costs (-£648 [95% CI -£874 to -£423]) than younger patients and quarterly health care costs were higher in patients with higher Charlson comorbidity scores (£146 [95% CI £112 to £180] per point). Costs were not substantially higher in patients with left ventricular dysfunction recorded (£230 [95% CI -£90 to £550]) and there was no strong evidence that costs differed by gender or in patients with a circulatory underlying cause of death.

Discussion:

Key findings

Healthcare use among people who die with or of HF increases sharply at the end of life. Younger patients receive the most costly care. Hospitalisation costs are the predominant health system costs, particularly during the last three months of life when they account for more than 90% of costs.

Many patients with HF spend protracted periods of time receiving care in hospital at the end of life and the majority (60%) die in hospital.

Comparison with other studies

Information on the economic impact of HF at the end of life is needed to judge whether the upfront costs of more intensive therapy (19, 20) might be justified by long-term savings due to reduced hospitalisations. However, high quality evidence on the healthcare costs of HF in the UK is scarce.

Stewart et al (21) used an aggregate 'top down' approach to estimate that the cost of primary, secondary and nursing home care for the UK population of patients with HF, which was £1.47 billion (3.83% of NHS expenditure) in 1995; hospitalisations accounted for 69% of this expenditure. We took a different 'bottom up' approach by identifying a cohort of patients with HF and used routinely collected data to measure their healthcare use and costs. Our approach has the advantage of providing greater detail on the types of healthcare used and the variation in healthcare use between patients and throughout the course of HF.

Our approach is similar to Kaul et al (22) who studied 47,970 patients with HF who died in Alberta between 2000 and 2006. They estimated that the mean cost per patient during the last 6 months of life was \$CAN 27,203 (approximately £6,600 per quarter at 2015 exchange rates) in 2006, which is in line with our result at the end of life (Figure 3). Farré et al (23), using routine data on all 88,195 individuals with HF identified in primary or secondary care in Catalonia, estimated an annual cost of

€6,571 (approximately £1,200 per quarter at 2015 exchange rates) which is similar to our estimate in the three to four years before death (Figure 3). In common with our findings, both studies reported higher costs in younger patients and in those with more comorbidities. Although device implantation was relatively uncommon in our cohort, more intensive therapy in younger patients may explain the association between costs and age. Kaul et al reported that the percentage of patients dying in hospital decreased from 60.4% in 2000 to 54.0% in 2006, compared to our observation of 59.9% in 2012/13. In common with previous research (24) we observed that the majority of hospitalisations, even at the end of life, were for comorbid non-cardiovascular conditions, most commonly kidney disease and respiratory problems. The high prevalence of these comorbidities may explain why healthcare costs were not higher in patients whose death was primarily attributed to circulatory disease.

Strengths and limitations

Our study presents novel evidence about the costs of healthcare among a relatively large population-based cohort of patients with HF for use by policy makers and researchers. We used three data sources (CPRD, HES and ONS) that have been extensively used and validated in previous research (9, 25). Since 2006/7 the Quality and Outcomes Framework (26) reimbursement scheme has given GPs incentives to maintain a HF register and confirm diagnoses by echocardiogram or specialist assessment. Therefore, recording of HF diagnoses from 2006/7 should be comprehensive. None of the data sources was primarily designed for economic research. We undertook extensive data cleaning to de-duplicate data and avoid double counting (e.g. multiple episodes in the same hospital spell). We mapped resource use to nationally representative unit costs that required a number of estimates and assumptions. We used a novel method to distinguish between the fixed and variable costs of hospital admissions, rather than using fixed HRG tariffs. Medications were costed according to BNF paragraph meaning that intra-paragraph variations in drug costs were overlooked. Given the relatively small cost of medications this is unlikely to be a major limitation.

We calculated the cost of healthcare for patients with HF and estimated how much that cost increased post-diagnosis. The HF codes used in the CPRD identify left ventricular dysfunction but are not specific enough to reliably differentiate HF with preserved or reduced ejection fraction. In the absence of a matched control group without HF, it was impossible to fully differentiate healthcare costs due to HF from costs due to other age-related comorbidities. We focussed on the last five years of life, when care is most expensive. An incidence cohort would be needed to fully capture all healthcare use from diagnosis to death. Using these routine datasets we cannot specify whether the medications prescribed followed clinical guidelines or reflected changes in laboratory test results. Our cost estimates are conservative and do not include direct care costs such as A&E attendances, nursing home, hospice and social care. Tanuseputro et al (27) estimated that long-term care and home care costs make up substantial proportions (15.5% and 8.3% respectively) of the total costs of healthcare during the last year of life. We did not measure the indirect impact on patients, carers and society due to morbidity and premature mortality. These productivity losses increase the total economic burden of HF by between 32.3% (28) and 66.2% (1). It has been reported that people diagnosed with HF use an additional 1.6 hours of informal caregiving per week compared to a matched control group (29).

Implications and future research

Our findings have clear implications for clinicians and managers on the importance of implementing evidence-based interventions to reduce avoidable hospital admissions. There is strong evidence that a number of interventions including appropriate pharmacotherapy, exercise-based rehabilitation, case management via telephone and home visits and multidisciplinary interventions before hospital discharge can substantially reduce HF readmission rates (30-32). However there are large gaps between guidelines and current practice; in the UK about one in ten patients receive cardiac rehabilitation and many do not receive cardiology or heart failure nurse follow up (4).

The high hospitalisation rate in the weeks preceding death has important implications for patient-centred care. Recognition of a transition point from active treatment towards palliative care is difficult, but vital in order to minimise recurrent hospitalisations at the end of life (33). Home palliative care services increase the probability of dying at home for those that wish to and have the potential to reduce costs, although evidence on cost-effectiveness is inconclusive (34).

Despite the high prevalence of HF, there is surprisingly little research on the economic impact on health systems, families and societies. Future research, particularly on residential care, informal care and productivity losses due to HF is needed and would strengthen the economic case for better prevention, diagnosis and treatment of this condition.

Conclusions

Healthcare costs increase sharply at the end of life and are dominated by hospital care. There is potential to save the health system money by better implementation of interventions that are known to reduce hospitalisations for HF, particularly at the end of life. Our data on the long-term costs of care should help researchers and policy makers to predict whether novel methods of diagnosis, monitoring and therapy will be cost-effective.

Tables:

Table 1 – Characteristics of the cohort

	HF cohort (N=1555)
Female; n (%)	737 (47.4)
Age at death; mean (SD; range)	83 (10; 24-105)
In hospital on date of death; n (%)	931 (59.9)
Underlying cause on death certificate; n (%)	
Circulatory system (ICD10 chapter IX)	895 (57.6)
Respiratory system (ICD10 chapter X)	273 (17.6)
Neoplasms (ICD10 chapter II)	157 (10.1)
Other	230 (14.8)
Years since HF diagnosis recorded; n (%)	
≤1 yr	617 (39.7)
1-≤2 yrs	319 (20.5)
2-≤3 yrs	204 (13.1)
3-≤5 yrs	180 (11.6)
>5 yrs	235 (15.1)
Left ventricular dysfunction*; n (%)	882 (56.7)
Co-morbidities; n (%)	
Renal disease	823 (52.9)
Chronic pulmonary disease	614 (39.5)
Diabetes	465 (29.9)
Cerebrovascular disease	448 (28.2)
Myocardial infarction	419 (27.0)
Peripheral vascular disease	373 (24.0)
Malignancy	352 (22.6)
Dementia	210 (13.5)
Diabetes with chronic complications	172 (11.1)
Charlson score; mean (SD; range)	5.16 (2.91; 0-18)
Region of residence; n (%)	
North West	354 (22.8)
South West	211 (13.6)
South Central	205 (13.2)
West Mid.	202 (13.0)
SE Coastal	160 (10.3)
London	160 (10.3)
East England	154 (9.9)
North East	46 (3.0)
Yorkshire & Humber	35 (2.3)
East Mid.	28 (1.8)

* Read codes: G581. Left ventricular failure; G5810 Acute left ventricular failure; 585f.

Echocardiogram shows left ventricular systolic dysfunction; 585g. Echocardiogram shows left ventricular diastolic dysfunction; G5yy9 Left ventricular systolic dysfunction; G5yyA Left ventricular diastolic dysfunction. ICD10 code I50.1 Left ventricular failure.

Table 2 – Frequency of cardiac hospital admissions and medications

Cardiac admissions - HRG label [primary diagnosis] (N=3,200)	n	%
HF or cardiogenic shock	1,124	35.1
[Congestive heart failure]	[779]	
[Left ventricular failure]	[193]	
[Heart failure unspecified]	[71]	
[Other]	[81]	
Non interventional acquired cardiac conditions*	443	13.8
Arrhythmia or Conduction Disorders	251	7.8
Actual or Suspected Myocardial Infarction	233	7.3
Catheter**	183	5.7
Implantable devices***	155	4.8
Syncope or Collapse	135	4.2
Cardiac Valve Disorders	52	1.6
Other	624	19.5
Non-cardiac admissions – HRG chapter (n=11,976)		
Urinary tract and male reproductive system	4,537	37.9
Respiratory system	1,579	13.2
Digestive system	1,158	9.7
Haematology, chemotherapy, radiotherapy & palliative	926	7.7
Musculoskeletal system	876	7.3
Other	2,900	24.2
Cardiovascular system medicinal products prescribed (N=365,554)	n	%
Diuretics	73,051	20.0
Hypertension and HF****	65,665	18.0
Antiplatelets	49,292	13.5
Nitrates, calcium channel blockers and other antianginal	48,429	13.3
Lipid regulating drugs	47,643	13.0
Beta-adrenoceptor blocking drugs	37,435	10.2
Anticoagulants and protamine	21,650	5.9
Positive inotropic drugs	17,772	4.9
Other	4,617	1.3

* HRG4 code removed after 2012/13

** Predominantly coronary angiography/arteriography

*** Including implantation of pacemaker (n=72); implantation of cardioverter defibrillator (n=26); renewal / resiting / removal of devices (n=38) and other procedures (n=20)

**** Including Vasodilator antihypertensive drugs; Centrally acting antihypertensive drugs; Adrenergic neurone blocking drugs; Alpha-adrenoceptor blocking drugs; Drugs affecting the renin-angiotensin system

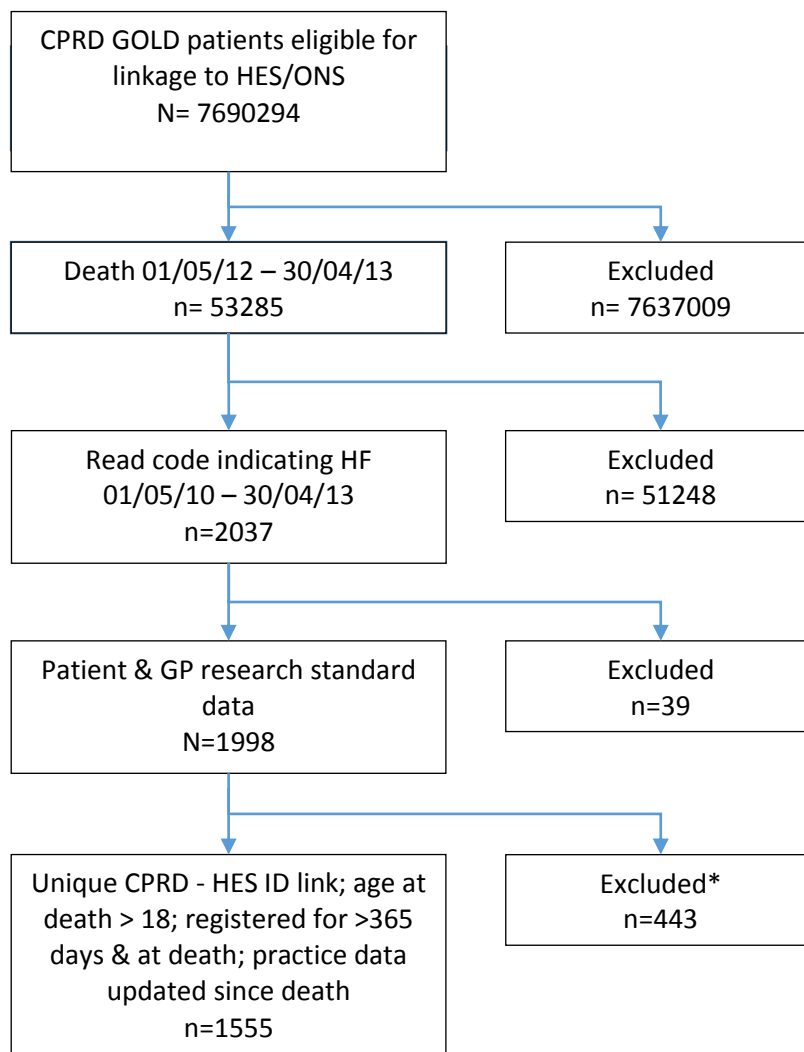
Table 3 – Health system costs by proximity to death, HF diagnosis and other characteristics

	HF cost model			Subgroup cost model		
	Coefficient	95% CI		Coefficient	95% CI	
Reference*	686	569	803	348	-38	735
Year 2	-23	-125	80	-18	-121	84
Year 3	216	81	351	227	93	362
Quarter 13	468	214	722	487	233	741
Quarter 14	201	-7	408	225	17	433
Quarter 15	369	140	598	398	170	627
Quarter 16	582	331	834	616	364	868
Quarter 17	780	518	1041	822	559	1084
Quarter 18	846	524	1168	894	571	1218
Quarter 19	2045	1624	2466	2102	1680	2524
Quarter 20	6702	6210	7193	6782	6289	7275
Post HF diagnosis	1439	1260	1619	1221	947	1495
Left ventricular dysfunction				230	-90	550
Charlson score				146	112	180
Female				108	-63	280
Age ≥75				-648	-874	-423
Circulatory death				-180	-360	1
R-sq	0.1378			0.1500		
Patients	1555			1555		
Observations	28923			28923		

* In the HF cost model the reference represents the average quarterly cost of healthcare in year 1, for patients who have not yet been diagnosed with HF. All other coefficients represent additional quarterly costs compared to this reference. For example the quarterly cost is £1,439 higher in patients who have been diagnosed with HF. In the subgroup cost model the reference represents the average quarterly cost of healthcare in year 1, for male patients aged less than 75, with a Charlson score of zero who have not yet been diagnosed with HF. All other coefficients represent additional quarterly costs compared to this reference.

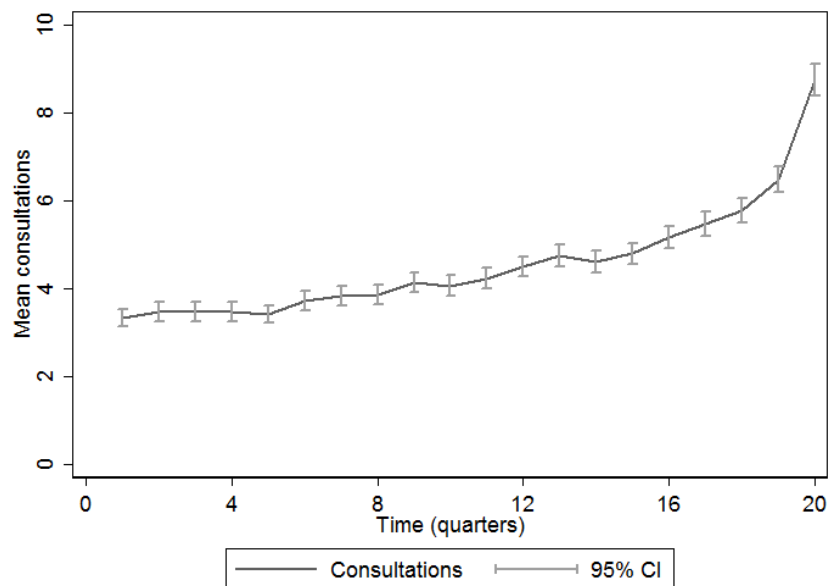
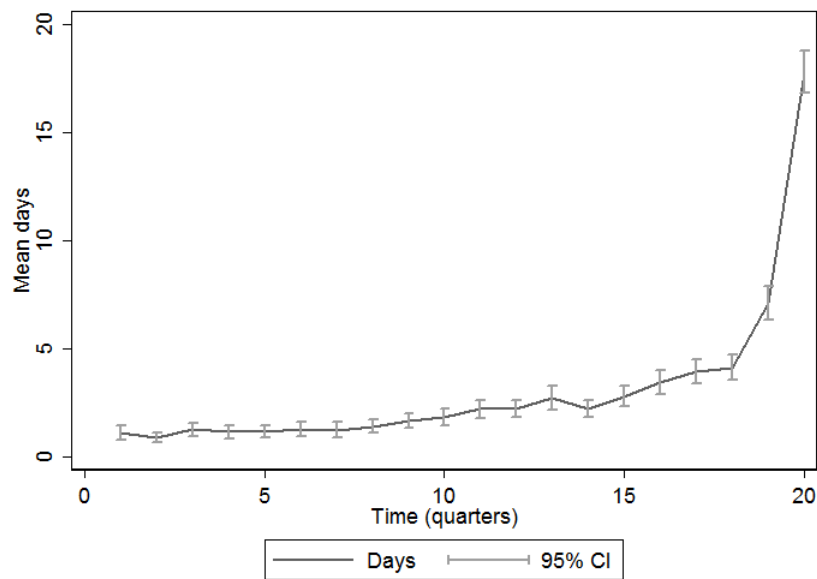
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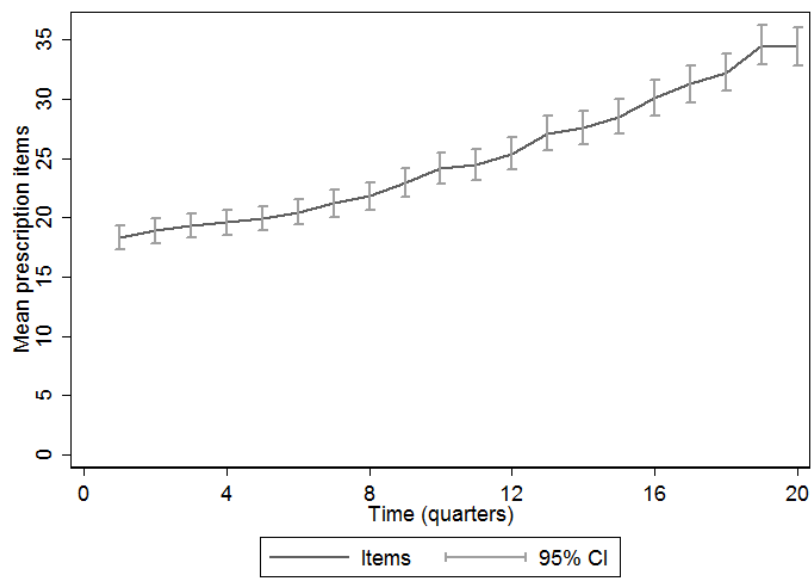
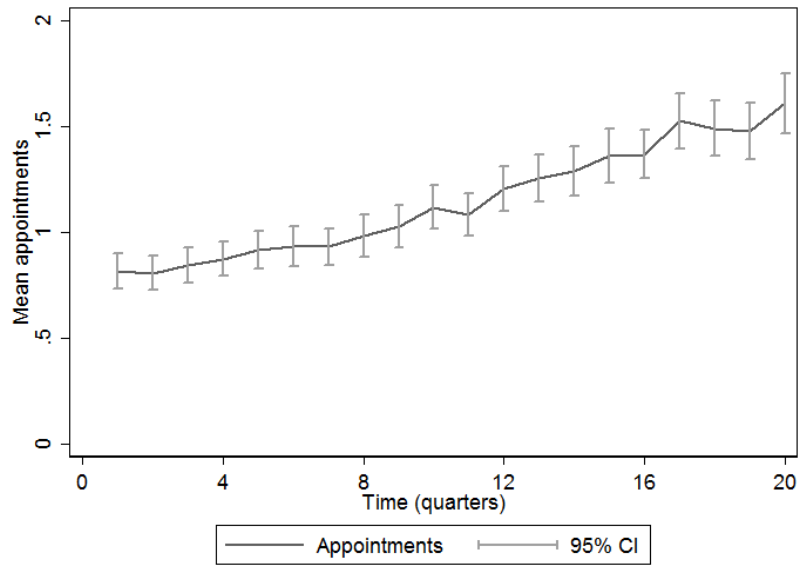
Figure 1 Patient selection flowchart



* 32 CPRD IDs removed due to more than one CPRD ID linked to a unique HES ID; 4 CPRD IDs removed as death < 18 years; 254 CPRD IDs removed as patient transferred out before death or practice data not updated since death; 153 CPRD IDs removed as patient registered with practice less than 1 year before death.

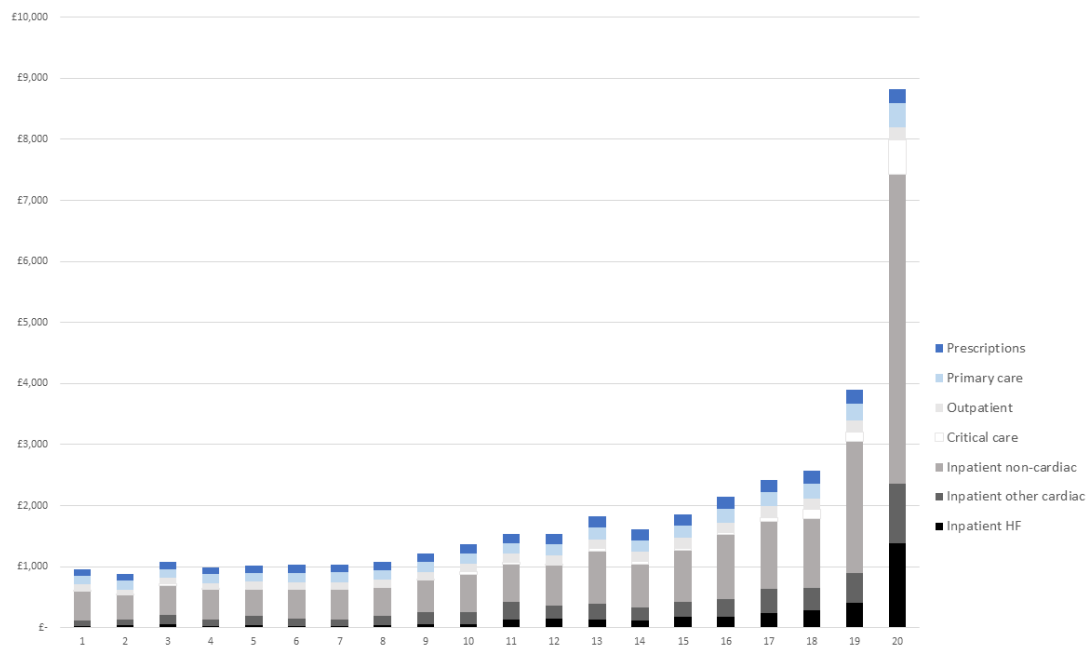
Figure 2 – Use of healthcare resources in 3 month periods (quarters) leading up to death (different y-axis scales)





- a) Days in hospital
- b) Outpatient appointments
- c) Primary care consultations
- d) Prescribed medicinal items

Figure 3 – Cost of primary and secondary care in 3 month periods (quarters) leading up to death



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